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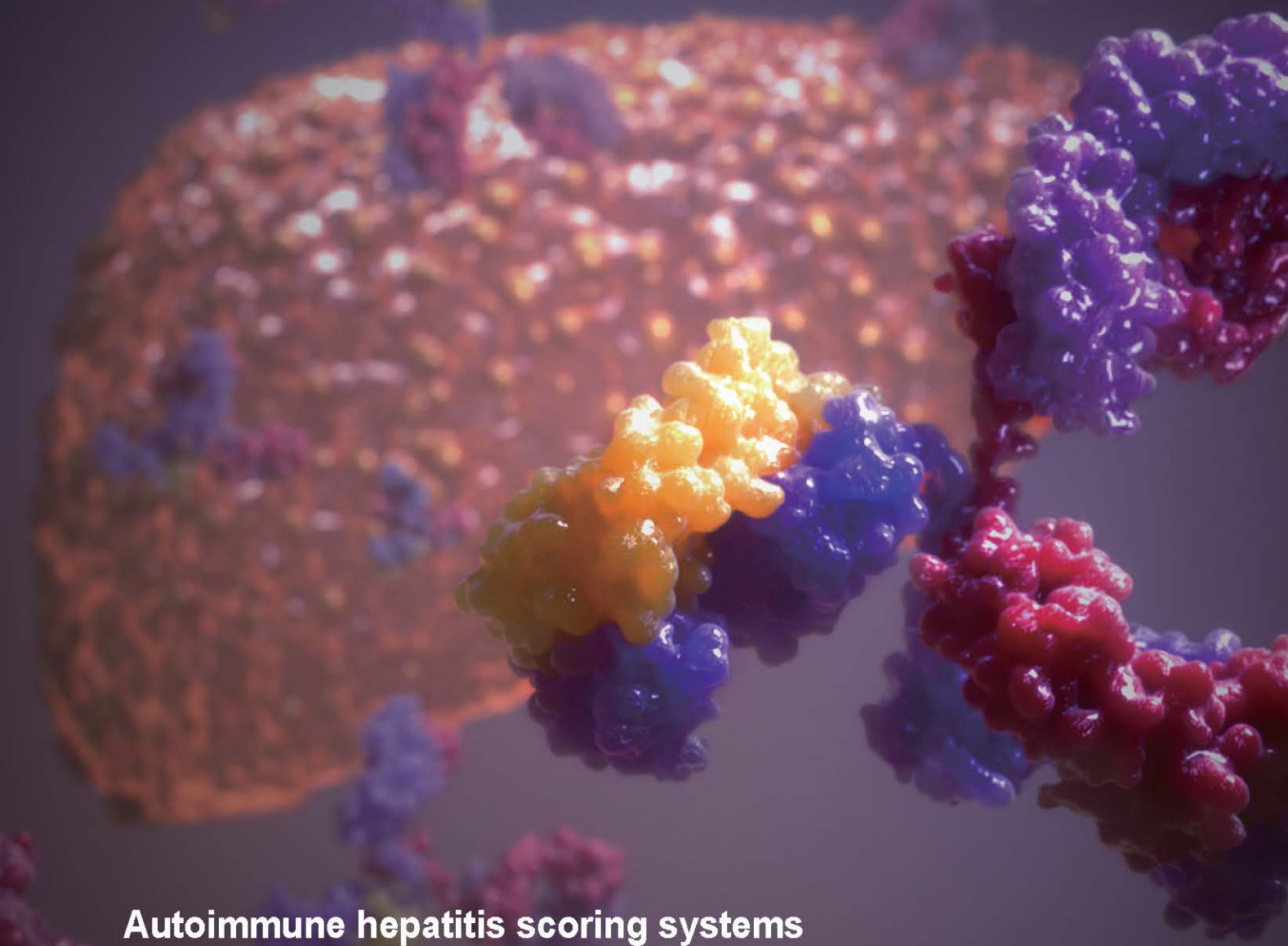

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Letter to the Editor

Letter regarding "Waiting for the changes after the adoption of steatotic liver disease"

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Dear Editor,

We read with interest the recent review by Yoon and Jun.[1] We further describe the challenges and limitations in the implementation of this shift to the new classification of steatotic liver disease (SLD)[2] in Asia.

SLD is the new umbrella term covering Metabolic Dysfunction-Associated SLD (MASLD), MetALD (MASLD and increased alcohol intake), alcohol-associated liver disease (ALD), specific aetiology and cryptogenic SLD,[2] and has been met with much debate.

However, discriminating between metabolic and alcohol-associated hepatic steatotic disorder is complex. The assessment of problematic alcohol use remains challenging due to limitations in alcohol intake assessment, lack of non-invasive diagnostic methods for alcohol-associated hepatitis,[3] and the unmet need to unify the definition of Metabolic Syndrome (MetS). There is notable discrepancy in the prevalence of MetS across different countries or territories, such as the United Kingdom (34.2%), Japan (25.2%), Taiwan (22.5%), and Italy (30.1%).[4] It is plausible that these variations arise in part from differences in diagnostic criteria employed. National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III), International Diabetes Foundation, World Health Organization, and European Group for the Study of Insulin Resistance, have put forth their own criteria for diagnosing MetS. Of particular relevance to Asia is the modified NCEP-ATP III guidelines, which propose lower waist circumference cut-off thresholds compared to standard NCEP-ATP III guidelines. In a Singapore study by Chan et al.[4] on the prevalence of MetS among psoriasis patients, utilizing the original criteria yielded a MetS prevalence of 33%, while application of the modified criteria raised this figure to 45.1%. This divergence in prevalence underscores the critical importance of consistent and standardized diagnostic criteria for MetS across different populations, as this significantly alters the epidemiological landscape of MetS.

This is in contradistinction to the high concordance rates of MASLD, non-alcoholic fatty liver disease (NAFLD) and metabolic-associated fatty liver disease (MAFLD) diagnoses.

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In a Hong Kong study of 277 participants with intrahepatic triglyceride content ≥5% on proton-magnetic resonance spectroscopy, 89.2% fulfilled criteria for all three definitions.[5] Among the NAFLD cases, only 2.3% and 5.4% failed to meet metabolic criteria of MASLD and MAFLD, respectively.

Recent studies on the genetic aetiology have revealed considerable overlap between MASLD and ALD. Specifically, variants in the genes *PNPLA3, TM6SF2,* and *MBOAT7* have been strongly associated with an increased risk for both conditions.[6] The *PNPLA3* I148M variant is the most widely validated genetic determinant and linked to severity of alcoholic cirrhosis in ALD. *TM6SF2* and *MBOAT7* variants have been reported to confer a risk for progressive disease in both metabolic dysfunction-associated steatohepatitis (MASH) and ALD. Furthermore, it has been shown that MASLD can be driven by endogenous production of ethanol derived from the microbiome.[7,8] These studies indicate the presence of shared biological pathways driving both metabolic and alcohol-related liver injury. These substantial overlaps challenge the binary framework often used to distinguish between metabolic and alcohol-related liver diseases.

The assimilation of the new terminology for SLD demands strategic interventions. Standardized alcohol consumption assessment, harmonized electronic medical records, integration of artificial intelligence,[9] and automatic flagging for MetS, represent significant avenues for clinical management. Employing a standardized radiological report, complemented by cues to categorise underlying risk factors for MASLD/MetALD/MASH, replacing "fatty" with more neutral terms like "lipid/cholesterol/oil," underscore the relevance of metabolic disorders and alcohol usage.

Adopting a pathogenesis-based approach is essential. This offers deeper insights into SLD's complexity, guiding tailored management strategies aligned with underlying causes. SLD nomenclature should also encompass other liver aetiologies.[10]

Social and nutrition prescribing have been recently lauded as promising avenues to address the social, economic and mental needs of obesity in MASLD.[11]Healthcare professionals refer to non-medical support systems rooted in the community (e.g., support groups, community gardening, music/culinary classes) with attention to the social determinants of health unique to the individual. There is much work for this to be contextualised for the Asian palate, for SLD programmes and community efforts to be streamlined, and for link workers (social prescribing coordinators) to gain familiarity and expertise in SLD case management. Healthy nutrition habits need to be ingrained systematically in early childhood education curriculum and national policies implemented such as front-of-pack labelling, workplace policies for employees with medically significant and risky SLD. Collectively, these strategies endeavour to streamline diagnostics, enrich medical comprehension, nurture heightened patient engagement, reduce clinical load of SLD at the specialist level and pave the way for prevention of liver diseases and success.

In conclusion, the recent progress in redefining the nomenclature and classification of SLD represents a significant advancement in our understanding of this prevalent and enigmatic conditions. The proposed shift towards a more affirmative and comprehensive approach has the potential to transform clinical practice and research paradigms in management of liver diseases. However, for Asia, the existing challenges in differentiation and accurate classification of SLD underscore the need for ongoing interdisciplinary collaboration, practical implementation and innovative diagnostic tools.

Authors' contributions

Conception or design of the work: Kuo Chao Yew, Hazel H. Oon. Drafting the article: Kuo Chao Yew, Sunny H. Wong, Hazel H. Oon. Critical revision of the article: All authors. Final approval of the version to be published: All authors.

Abbreviations:

SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; MetALD, metabolic dysfunction-associated steatotic liver disease and increased alcohol intake; ALD, alcohol-associated liver disease; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; MAFLD, metabolic-associated fatty liver disease; MASH, metabolic dysfunction-associated steatohepatitis

Conflicts of Interest

Kuo Chao Yew: speaker for Gilead Sciences and AbbVie, clinical investigator for AstraZeneca.

Sunny H. Wong: Advisory committee member for Groken Biosciences, Biocodex, and Aptorum Group Limited; speaker for Janssen and AstraZeneca.

Vincent W. Wong: advisory committee member for AbbVie, Boehringer Ingelheim, Echosens, Gilead Sciences, Intercept, Inventiva, Merck, Novo Nordisk, Pfizer, Sagimet Biosciences and TARGET Pharma Solutions; speaker for Abbott, AbbVie, Gilead Sciences, Novo Nordisk and Unilab. Received a research grant from Gilead Sciences and is a cofounder of Illuminatio Medical Technology.

Hazel H. Oon: speaker, advisory board member and researcher for AbbVie, Galderma, Janssen and Novartis. Clinical investigator for Pfizer, advisory board member for Amgen, speaker and advisory board member for Boehringer Ingelheim and Eli Lilly.

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